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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/987,485	11/14/2001	Michael A. Barry	15987/282434	7070

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/987,485	Applicant(s) BARRY ET AL.	
	Examiner Bao Qun Li	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-9 and 15-17* is/are pending in the application.

4a) Of the above claim(s) *7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *7* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence requirment* .

DETAILED ACTION

The response to Office Action on ***Election/Restrictions*** requirement has been acknowledged. Claims 5-6, 10-14 and 18-36 have been canceled. Claims 1-4, 7-9 and 15-17 are pending.

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-4, 7-9 and 15-17 in scope of PSTCD peptide Paper No. 10 has been acknowledged. The traversal is on the ground(s) that the selection of each biotinylation-competent protein or peptide should be considered as a species election because it belongs to the genus of biotinylated protein or peptide.

2. Applicants' argument has been respectfully considered. However, it is not found persuasive because each biotinylation competent protein or peptide is structural and functionally different molecule, which requires different search. Furthermore, each kind of fusion protein made by different biotinylation competent protein or peptide has different patentable weight and constitutes different invention.

3. Regarding to claim 7, Applicants' representative Michael A. Sanzo was contacted. During a telephone conversation with Michael A. Sanzo on June 27, 2003 a provisional election was made with traverse to restricting the claim 5 into another non-elected group and prosecute the invention of Group I, claims 1-4,8-9 and 15-17 . Affirmation of this election must be made by applicant in replying to this Office action. Claim 7 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. Claims 1-4, 8-9 and 15-17 in scope of PSTCD peptide are considered before the examiner.

5. Applicants are reminded to amend claims 1-4, 8-9 and 15-17 within the scope of PSTCD peptide for reflecting the examination on the merits.

6. Applicants also reminded to cancel claim 8 drawn to the non-elected group.

Sequence requirements

7. This application contains sequence disclosures **in Figure 1** that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and

(a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

8. Full compliance with the sequence rules by **filling a sequence identification number in the figure legend of Figure 1 or in the drawing** is required in response to this Office Action. A complete response to this office action should include both compliance with the sequence rules and a response to the Office Action set forth below. Failure to fully comply with **both** these requirements in the time period set forth in this office action will be held non-responsive

Oath/Declaration

9. This is to clarify that the name and registration number of undersigned power attorney of current application, Micheal A. Sanzo has been found in lines 7-8 on the last paragraph of PAGE 2 OF DELARATION AND POWER OF ATTORNEY filed on March 11, 2002.

Claim Objections

10. Claim 2 is objected to because of the following informalities: Please spell out the complete word of PSTD in claim 2 when it first appears in the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 2 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claim 2-3 are unclear in that the structural characteristic of the PSTCD peptide are not defined because the claims fail to define the orientation of cited lysine 89 and at least 63 amino

acids of a PSTCD peptide. Because every amino acid sequence has two ends, a numerical order from the N-terminal will be different if it is counted from N-terminus from it is counted from the C-terminus. Therefore, claims are considered as indefinite unless Applicants amend the claims to clarify the orientation of the amino acid numerical order.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 2 and 3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for having a fusion protein made by P. Schermanii transcarboxylase (PSTCD) fused with a viral antigen polypeptide at its C-terminus, wherein the PSTCD peptide is either in a full length or portion of PSTCD of SEQ ID NO: 2, does not reasonably provide enablement for having a fusion protein made by at least any 63 amino acids of PSTCD peptide and amino acid lysine at the position of 89, wherein the fusion protein is able to undergo biotinylation when it is expressed in a host cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

16. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and gain in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988). These factors include the following:

17. 1) & 2) State of art and unpredictability of the field.

18. The method for making a fusion protein undergoing post translational biotinylation by using PSTCD peptide, wherein the peptide must contains the lysin at the position 89 from the N-terminus and at lease 66 contiguous amino acids from the C-terminus. However, it is unpredictable if you use any PSTCD peptide with any 63 amino acids in length and having a deletion from is C-terminus because the art teaches that the deletion of two amino acids from C-terminus will completely abolish the biotinylation process of the fusion protein as evidenced by Stolz et al. (FEBD Letter 1998, Vol. 440, pp. 213-217, see lines 16-20 on 1st col. Of page 216).

19. 3) & 4) Number of working examples and amount of guidance presented in the specification.

20. Applicants only teach that a fusion protein comprising a full length of PSTCD of SEQ ID NO: 1 or portion of PSTCD of SEQ ID NO: 2 fused with a viral antigen polypeptide, preferably an adenovirus fiber protein at its C-terminus, is able to undergo biotinylation when they are expressed in a host cell line.

21. However, the full length of PSTCD is 122 amino acids in length, if you would like to have 63 amino acids in length that covers the lysine at the position 89 from the N-terminus of the full length PSTCD peptide, you probably can generate considerable amount of such peptides. The specification does not demonstrate that any fusion protein made by all 63 amino acids of PSTCD peptides that fuses with a polypeptide of interest in its C-terminus, as long as the PSTCD peptide contains lysine at the position 89, are all able to undergo biotinylation when the fusion protein is expressed in a host cell. Especially if the 63 amino acids fragment of PSTCD which has C-terminal amino acid residues deletion.

22. 5) Scope of the claims.

23. The scope of claimed invention broadly read on a biotinylated fusion protein comprising PSTCD peptide and a polypeptide, wherein the PSTCD peptide is made by using any 63 amino acids of PSTCD fragment as long as the PSTCD peptide containing the lysine at the position 89.

24. 6) & 7) Nature of the invention and lever of the skill in the art.

25. The nature of invention is related to a fusion protein having a property of undergoing biotinylation when it is expressed in a host cell. The invention involves the high technology of molecular biology and protein chemistry.

26. Given the above analysis of the factors which the courts have determined are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan would have to conduct undue and excessive experimentation in order to practice the full scope of the claimed invention.

Claim Rejections - 35 USC § 102

27. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

28. Claims 1-3 and 15-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Cronan et al. (US Patent No. 5,252,466A).

29. Cronan et al. teach a method for making a bitinylated fusion protein expressed by transfecting a recombinant vector into a host cell, wherein the vector comprises a signal or a leader sequence and a hybridized DNA sequence encoding a fusion protein of β-galactosidase fused with a amino acid sequence of 1.3 S subunit of P. Schermanii transcarboxylase (PSTCD), in which the PSTCD peptide contains a fragment having 100% identical amino acid sequence to the claimed PSTCD peptide of SEQ ID NO: 2, wherein the said PSTCD peptide is able to undergo biotinylation when it is expressed in the host cell E Coli. For example, a 75 amino acids or a 106 amino acids peptide of PSTCD from its C –terminus. All of these fragments comprise lysine at position of 89 and at least 63 amino acids and they are joined to the polypeptide at its C-terminus (Fig. 21, and line 32 on col. 19 through the lie 15 on col. 22, especially see lines 32-42 on col. 19). Though they are no exactly 70 amino acids in length; some of the fragments have 100% homology to the claimed PSTCD fragment of SEQ ID NO: 2. The DNA construct of the expression vector further comprises a signal sequence or signal-leader sequence, which is a sequence of amino acids at the amino terminus of a polypeptide, which provides for secretion of the protein or polypeptide from the cell in which it is produced (See lines 18-49 on col. 11). Variety sizes of these fusion proteins have been expressed by using these constructs (See Fig.

20). Because claims 1-3 and 15-16 do not limit the PSTCD peptide as SEQ ID NO: 2, it opens the claimed fragments as any fragment of PSTCD as long as it is a portion of PSTCD with lysin at the position of 89 and has at least 63 amino acids in length . Therefore, the claimed invention is anticipated by the cited reference.

30. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Cress et al. (EP 0 511 747A1).

31. Cress et al. disclose a recombinant polypeptide that is a fusion protein comprising an avidin-binding polypeptide with an attached interest polypeptide at its C-terminus, wherein the avidin-binding polypeptide is a 1.3S subunit of PSTCD peptide with 100% homology to the claimed SEQ ID NO: 1 of claimed "PSTCD" peptide or a portion of said avidin-biding polypeptide that contains a biotin attachment domain with at least a sequence including lysine at the position 89 and undergoes biotinylation when expressed in a host E Coli cell (See entire document, especially claims 1-16). While the avidin –binding polypeptide disclosed by Cress et al. is named differently from that of current application; considering the avidin-binding polypeptide taught by Cress et al. has an identical structure and same biological function to the claimed biotinalytion-competent polypeptide, the claimed invention is anticipated by the cited reference.

Conclusion

Claims 1-3 and 15-16 are not allowable.

Claims 4, 8-9 and 17 are directed to a fusion protein, which is able to undergo biotinylation when it is expressed in a host cell and consists of the PSTCD peptide of SEQ ID NO: 2 and a viral surface protein. This subject matter is found to be free from prior art. The closest prior art only teach that a fusion protein with property of undergoing biotinylation can be made with PSTCD peptide and a β-galactosidase, wherein the PSTCD comprises at least 66 amino acid residues in length from the C-terminus and it must contains the lysine at the position 89 from the N-terminus of the full length PSTCD peptide. However, no prior art has taught or suggested that a fusion protein with a property of undergoing biotinylation when it is expressed in a host cell consisting of absolute SEQ ID NO: 2 and a viral surface protein. However, the

claims are not in allowable condition since they are dependent on the rejected claims. The claims would be allowed if they were written in an independent form with all limitations identified by Office supra.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 7:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li
June 29, 2003